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☐ 1: [P31327](#). Reports ...[gi:4033707]

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LOCUS P31327 1500 aa linear PRI 12-DEC-2006

DEFINITION Carbamoyl-phosphate synthase [ammonia], mitochondrial precursor (Carbamoyl-phosphate synthetase I) (CPSase I).

ACCESSION P31327

VERSION P31327 GI:4033707

DBSOURCE swissprot: locus CPSM_HUMAN, accession [P31327](#);
 class: standard.
 extra accessions: O43774, Q7Z5I5
 created: Jul 1, 1993.
 sequence updated: Dec 15, 1998.
 annotation updated: Dec 12, 2006.
 xrefs: [D90282.1](#), [BAA14328.1](#), [Y15793.1](#), [CAA75785.1](#), [AF154830.1](#),
[AAD38072.1](#), [AY317138.1](#), [AAP84318.1](#), [AY167007.1](#), [AAO31763.1](#),
[AY166970.1](#), [AY166971.1](#), [AY166972.1](#), [AY166973.1](#), [AY166974.1](#),
[AY166975.1](#), [AY166976.1](#), [AY166977.1](#), [AY166978.1](#), [AY166979.1](#),
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[AY167000.1](#), [AY167001.1](#), [AY167002.1](#), [AY167003.1](#), [AY167004.1](#),
[AY167005.1](#), [AY167006.1](#), [AF536523.1](#), [AAN77181.1](#), [BX640601.1](#),
[CAE45707.1](#), [JQ1348](#)
 xrefs (non-sequence databases): UniGene:Hs.149252, HSSP:P00968,
 IntAct:P31327, GermOnline:ENSG00000021826, Ensembl:ENSG00000021826,
 KEGG:hsa:1373, HGNC:2323, HPA:CAB003781, MIM: [237300](#), MIM: [608307](#),
 BioCyc:MetaCyc:MONOMER-11364, Reactome:REACT_13.1,
 ArrayExpress:P31327, RZPD-ProtExp:IOH12892, GO:0005739, GO:0004087,
 GO:0005515, InterPro:IPR011761, InterPro:IPR013816,
 InterPro:IPR006275, InterPro:IPR006274, InterPro:IPR001317,
 InterPro:IPR002474, InterPro:IPR005483, InterPro:IPR005480,
 InterPro:IPR005481, InterPro:IPR005479, InterPro:IPR011702,
 InterPro:IPR000991, InterPro:IPR011607, InterPro:IPR013817,
 Pfam:PF00289, Pfam:PF02786, Pfam:PF02787, Pfam:PF00988,
 Pfam:PF00117, Pfam:PF02142, PRINTS:PR00098, PRINTS:PR00099,
 PRINTS:PR00096, TIGRFAMs:TIGR01369, TIGRFAMs:TIGR01368,
 PROSITE:PS50975, PROSITE:PS00866, PROSITE:PS00867

KEYWORDS Acetylation; Allosteric enzyme; Alternative splicing; ATP-binding;
 Disease mutation; Ligase; Mitochondrion; Nucleotide-binding;
 Polymorphism; Repeat; Transit peptide; Urea cycle.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 1500)

AUTHORS Haraguchi,Y., Uchino,T., Takiguchi,M., Endo,F., Mori,M. and Matsuda,I.

TITLE Cloning and sequence of a cDNA encoding human carbamyl phosphate synthetase I: molecular analysis of hyperammonemia
JOURNAL Gene 107 (2), 335-340 (1991)
PUBMED [1840546](#)
REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), AND VARIANTS SER-1266; LEU-1283 AND ASN-1406.
TISSUE=Liver

REFERENCE 2 (residues 1 to 1500)
AUTHORS Finckh,U., Kohlschutter,A., Schafer,H., Sperhake,K., Colombo,J.P. and Gal,A.
TITLE Prenatal diagnosis of carbamoyl phosphate synthetase I deficiency by identification of a missense mutation in CPS1
JOURNAL Hum. Mutat. 12 (3), 206-211 (1998)
PUBMED [9711878](#)
REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), VARIANT CPS1 DEFICIENCY MET-544, AND VARIANT ALA-344.
TISSUE=Liver

REFERENCE 3 (residues 1 to 1500)
AUTHORS Summar,M.L., Hall,L.D., Eeds,A.M., Hutcheson,H.B., Kuo,A.N., Willis,A.S., Rubio,V., Arvin,M.K., Schofield,J.P. and Dawson,E.P.
TITLE Characterization of genomic structure and polymorphisms in the human carbamyl phosphate synthetase I gene
JOURNAL Gene 311, 51-57 (2003)
PUBMED [12853138](#)
REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), AND VARIANTS ALA-344; SER-1376 AND ASN-1406.

REFERENCE 4 (residues 1 to 1500)
AUTHORS Huo,R., Zhu,H., Huang,X.Y., Xu,Z.Y., Lu,L., Xu,M., Yin,L.L., Li,J.M., Zhou,Z.M. and Sha,J.H.
TITLE Direct Submission
JOURNAL Submitted (??-JUN-2003)
REMARK NUCLEOTIDE SEQUENCE (ISOFORM 2).
TISSUE=Testis

REFERENCE 5 (residues 1 to 1500)
AUTHORS Funghini,S., Donati,M.A., Pasquini,E., Zammarchi,E. and Morrone,A.
TITLE Structural organization of the human carbamyl phosphate synthetase I gene (CPS1) and identification of two novel genetic lesions
JOURNAL Hum. Mutat. 22 (4), 340-341 (2003)
PUBMED [12955727](#)
REMARK NUCLEOTIDE SEQUENCE (ISOFORM 1), VARIANTS CPS1 DEFICIENCY GLY-457 AND ARG-810, AND VARIANT ASN-1406.

REFERENCE 6 (residues 1 to 1500)
AUTHORS Haeberle,J., Schmidt,E., Pauli,S., Rapp,B., Christensen,E., Wermuth,B. and Koch,H.G.
TITLE Gene structure of human carbamylphosphate synthetase 1 and novel mutations in patients with neonatal onset
JOURNAL Hum. Mutat. 21, 444-444 (2003)
PUBMED [12655559](#)
REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM 1), AND VARIANTS CPS1 DEFICIENCY SER-843 AND GLU-875.

REFERENCE 7 (residues 1 to 1500)
CONSRM The German cDNA consortium
TITLE Direct Submission
JOURNAL Submitted (??-AUG-2003)
REMARK NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] OF 795-1500.
TISSUE=Small intestine

REFERENCE 8 (residues 1 to 1500)
AUTHORS Aoshima,T., Kajita,M., Sekido,Y., Kikuchi,S., Yasuda,I., Saheki,T., Watanabe,K., Shimokata,K. and Niwa,T.
TITLE Novel mutations (H337R and 238-362del) in the CPS1 gene cause carbamoyl phosphate synthetase I deficiency
JOURNAL Hum. Hered. 52 (2), 99-101 (2001)
PUBMED [11474210](#)
REMARK VARIANT CPS1 DEFICIENCY ARG-337.

REFERENCE 9 (residues 1 to 1500)
 AUTHORS Pearson,D.L., Dawling,S., Walsh,W.F., Haines,J.L., Christman,B.W., Bazyk,A., Scott,N. and Summar,M.L.
 TITLE Neonatal pulmonary hypertension--urea-cycle intermediates, nitric oxide production, and carbamoyl-phosphate synthetase function
 JOURNAL N. Engl. J. Med. 344 (24), 1832-1838 (2001)
 PUBMED [11407344](#)
 REMARK VARIANT ASN-1406.
 COMMENT On or before Mar 15, 2005 this sequence version replaced gi:[87018](#), gi:[399296](#).
 [FUNCTION] Involved in the urea cycle of ureotelic animals where the enzyme plays an important role in removing excess ammonia from the cell.
 [CATALYTIC ACTIVITY] 2 ATP + NH(3) + CO(2) + H(2)O = 2 ADP + phosphate + carbamoyl phosphate.
 [ENZYME REGULATION] Requires N-acetylglutamate as an allosteric activator.
 [INTERACTION] P10398:ARAF; NbExp=3; IntAct=EBI-536811, EBI-365961; P04049:RAF1; NbExp=2; IntAct=EBI-536811, EBI-365996.
 [SUBCELLULAR LOCATION] Mitochondrion.
 [ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named isoforms=2; Name=1; IsoId=P31327-1; Sequence=Displayed; Name=2; IsoId=P31327-2; Sequence=VSP_009332; Note=No experimental confirmation available.
 [TISSUE SPECIFICITY] Primarily in the liver and small intestine.
 [DOMAIN] The type-1 glutamine amidotransferase domain is defective.
 [DISEASE] Defects in CPS1 are the cause of CPS1 deficiency [MIM:237300]; an autosomal recessive metabolic disorder that cause a type of hyperammonemia. Clinical symptoms are vomiting in infancy, protein intolerance, intermittent ataxia, seizures, lethargy, and mental retardation.
 [SIMILARITY] Contains 2 ATP-grasp domains.
 [SIMILARITY] Contains 1 type-1 glutamine amidotransferase domain.
 [WEB RESOURCE] NAME=GeneReviews;
 URL='http://www.genetests.org/query?gene=CPS1'.

FEATURES	Location/Qualifiers
source	1..1500 /organism="Homo sapiens" /db_xref="taxon: 9606 "
gene	1..1500 /gene="CPS1"
Protein	1..1500 /gene="CPS1" /product="Carbamoyl-phosphate synthase [ammonia], mitochondrial precursor" /EC_number=" 6.3.4.16 "
Region	1..451 /gene="CPS1" /region_name="Splicing variant" /experiment="experimental evidence, no additional details recorded" /note="Missing (in isoform 2). /FTId=VSP_009332."
Region	1..38 /gene="CPS1" /region_name="Transit peptide" /inference="non-experimental evidence, no additional details recorded" /note="Mitochondrion (By similarity)."
Region	39..1500 /gene="CPS1" /region_name="Mature chain" /experiment="experimental evidence, no additional details recorded" /note="Carbamoyl-phosphate synthase [ammonia]."

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" /FTId=PRO_0000029897."
  Region 39..219
    /gene="CPS1"
    /region_name="Region of interest in the sequence"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="Anthranilate phosphoribosyltransferase homolog."
  Region 43..404
    /gene="CPS1"
    /region_name="CarA"
    /note="Carbamoylphosphate synthase small subunit [Amino
    acid transport and metabolism / Nucleotide transport and
    metabolism]; COG0505"
    /db_xref="CDD:30851"
  Region 44..191
    /gene="CPS1"
    /region_name="CPSase_sm_chain"
    /note="Carbamoyl-phosphate synthase small chain, CPSase
    domain; pfam00988"
    /db_xref="CDD:41060"
  Site 55
    /gene="CPS1"
    /site_type="modified"
    /inference="non-experimental evidence, no additional
    details recorded"
    /note="N6-acetyllysine (By similarity).".
  Region 111
    /gene="CPS1"
    /region_name="Conflict"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="A -> S (in Ref. 1).".
  Site 119
    /gene="CPS1"
    /site_type="modified"
    /inference="non-experimental evidence, no additional
    details recorded"
    /note="N6-acetyllysine (By similarity).".
  Region 220..410
    /gene="CPS1"
    /region_name="Region of interest in the sequence"
    /experiment="experimental evidence, no additional details
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    /note="Glutamine amidotransferase-like."
  Region 220..395
    /gene="CPS1"
    /region_name="GATase1_CPSase"
    /note="This group of sequences represents the small chain
    of the glutamine-dependent form of carbamoyl phosphate
    synthase, CPSase II; cd01744"
    /db_xref="CDD:28856"
  Region 279
    /gene="CPS1"
    /region_name="Conflict"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="R -> Q (in Ref. 1).".
  Site 287
    /gene="CPS1"
    /site_type="modified"
    /inference="non-experimental evidence, no additional
    details recorded"
    /note="N6-acetyllysine (By similarity).".
  Region 337

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    /region_name="Variant"
    /experiment="experimental evidence, no additional details
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    /note="H -> R (in CPS1 deficiency). /FTId=VAR_014077."
Region 338
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    /region_name="Conflict"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="G -> C (in Ref. 1)."
Region 344
    /gene="CPS1"
    /region_name="Variant"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="T -> A (in dbSNP:rs1047883). /FTId=VAR_006834."
Region 421..544
    /gene="CPS1"
    /region_name="CPSase_L_chain"
    /note="Carbamoyl-phosphate synthase L chain, N-terminal
    domain; pfam00289"
    /db_xref="CDD:40385"
Region 437..822
    /gene="CPS1"
    /region_name="CarB"
    /note="Carbamoylphosphate synthase large subunit (split
    gene in MJ) [Amino acid transport and metabolism /
    Nucleotide transport and metabolism]; COG0458"
    /db_xref="CDD:30806"
Region 457
    /gene="CPS1"
    /region_name="Variant"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="V -> G (in CPS1 deficiency). /FTId=VAR_017562."
Site 527
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    /site_type="modified"
    /inference="non-experimental evidence, no additional
    details recorded"
    /note="N6-acetyllysine (By similarity)."
Region 544
    /gene="CPS1"
    /region_name="Variant"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="T -> M (in CPS1 deficiency). /FTId=VAR_006835."
Region 551..743
    /gene="CPS1"
    /region_name="Domain"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="ATP-grasp 1."
Region 718..722
    /gene="CPS1"
    /region_name="Conflict"
    /experiment="experimental evidence, no additional details
    recorded"
    /note="RLSRS -> KMSPN (in Ref. 1)."
Region 729
    /gene="CPS1"
    /region_name="Conflict"
    /experiment="experimental evidence, no additional details

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recorded"
/note="A -> T (in Ref. 1)."
Region 749
/gene="CPS1"
/region_name="Conflict"
/experiment="experimental evidence, no additional details
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/note="E -> G (in Ref. 1)."
Region 810
/gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details
recorded"
/note="Q -> R (in CPS1 deficiency). /FTId=VAR_017563."
Region 839..962
/gene="CPS1"
/region_name="CPSase_L_D3"
/note="Carbamoyl-phosphate synthetase large chain,
oligomerisation domain; pfam02787"
/db_xref="CDD:42743"
Site 841
/gene="CPS1"
/site_type="modified"
/inference="non-experimental evidence, no additional
details recorded"
/note="N6-acetyllysine (By similarity)."
Region 843
/gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details
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/note="L -> S (in CPS1 deficiency). /FTId=VAR_017564."
Region 875
/gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details
recorded"
/note="K -> E (in CPS1 deficiency). /FTId=VAR_017565."
Site 892
/gene="CPS1"
/site_type="modified"
/inference="non-experimental evidence, no additional
details recorded"
/note="N6-acetyllysine (By similarity)."
Region 912
/gene="CPS1"
/region_name="Conflict"
/experiment="experimental evidence, no additional details
recorded"
/note="F -> L (in Ref. 6)."
Region 977..1086
/gene="CPS1"
/region_name="CPSase_L_chain"
/note="Carbamoyl-phosphate synthase L chain, N-terminal
domain; pfam00289"
/db_xref="CDD:40385"
Region 979..1362
/gene="CPS1"
/region_name="CarB"
/note="Carbamoylphosphate synthase large subunit (split
gene in MJ) [Amino acid transport and metabolism /
Nucleotide transport and metabolism]; COG0458"
/db_xref="CDD:30806"
Region 1093..1284

Region /gene="CPS1"
/region_name="Domain"
/experiment="experimental evidence, no additional details recorded"
/note="ATP-grasp 2."
1161..1162

Region /gene="CPS1"
/region_name="Conflict"
/experiment="experimental evidence, no additional details recorded"
/note="EH -> AT (in Ref. 1)."
1204..1205

Region /gene="CPS1"
/region_name="Conflict"
/experiment="experimental evidence, no additional details recorded"
/note="GD -> EN (in Ref. 1)."
1254

Region /gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details recorded"
/note="I -> N (in Ref. 1)."
1266

Region /gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details recorded"
/note="F -> S (in dbSNP:rs1047886). /FTId=VAR_017566."
1283

Site /gene="CPS1"
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/inference="non-experimental evidence, no additional details recorded"
/note="M -> L (in dbSNP:rs1047887). /FTId=VAR_017567."
1291

Region /gene="CPS1"
/region_name="Conflict"
/experiment="experimental evidence, no additional details recorded"
/note="N6-acetyllysine (By similarity)."
1303

Region /gene="CPS1"
/region_name="MGS_CPS_I_III"
/note="Methylglyoxal synthase-like domain found in pyr1 and URA1-like carbamoyl phosphate synthetases (CPS), including ammonia-dependent CPS Type I, and glutamine-dependent CPS Type III; cd01423"
/db_xref="CDD:29635"
1360..1475

Region /gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details recorded"
/note="A -> V (in Ref. 1)."
1376

Region /gene="CPS1"
/region_name="Variant"
/experiment="experimental evidence, no additional details recorded"
/note="G -> S. /FTId=VAR_017568."
1406

/experiment="experimental evidence, no additional details recorded"

/note="T -> N (30-40% higher activity; risk factor for persistent pulmonary hypertension of the newborn; dbSNP:rs7422339). /FTId=VAR_017569."

ORIGIN

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1 mtriltafkv vrtlktgfgf tnvtahqkwk fsrpgirlls vkaqtahivl edgtkmkgys
61 fghpssvage vvfntglggy peaitdpayk ggiltmanpi ignggapdt aldelglsky
121 lesngikvsg llvldyskdy nhwlatkslg qwlqeeqvpa iygvdttrmlt kiirdkgtml
181 gkiefeggpv dfvdpnkqnl iaevstkdvk vygkgnptkv vavdcgiknn virllvkrge
241 evhlvpwnhd ftkmeydgil iagggpnpal aepliqrnrk ilesdrkepl fgistgnlit
301 glaagaktyk msmanrgqnq pvlntnkqa fitaqnhgya ldntlpagwk plfvnvndqt
361 negimheskp ffavqfhpev tpgpidteyl fdsffslikk gkattitsvl pkpalvasrv
421 evskvlilgs gglsigqage fdysgsqavk amkeenvktv lmpniasvq tnevglkqad
481 tvyflpitpq fvtevikaeq pdglilgmvg qtalncgvel fkrqvlkeyg vkvlgtaves
541 imatedrqlf scklneinek iapsfavesi edalkaadti gypvmirsay algglgsgic
601 pnretlmdls tkafamtnqi lveksvtgwk eieyevvrda ddncvtvcnm envdamgvht
661 gdsvvvapaq tlnaefqml rrtsinvrh lgivgecniq falhptsmev ciievnarls
721 rssalaskat gyplafiaak ialgiplpei knvvsgktsa cfepsldymv tkiprwdldr
781 fhgtssrigs smksvgevma igrfteesf kalrmchpsi egftprlpnm kewpsnldlr
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901 eetlkrakei gfsdkqiskc lglteaqtrelrlkknihpw vkqidtlaae ypsvtnylyv
961 tyngqehdvn fddhgmmvlg cgpyhigssv efdwcavssi rtrqlgkkt vvvncnpetv
1021 stdfdecckl yfeelsleri ldiyhqeacg gciisvggqi pnnlavplyk ngvkingtsp
1081 lqidraedrs ifsavldelk vaqapwkavn tlnealefak svdypcllrp syvlsgsamn
1141 vvfse demkk fleeatrvsq ehpvvltkfv egarevemda vgkdgrvish aisehvedag
1201 vhs gdatlml ptqtisqgai ekvkdatrki akafaisgpf nvqflvkgnd vlviecnlra
1261 srsfpfvskt lgvdfidvat kvmigenvde khlptldhpi ipadyvaika pmfswprlrd
1321 adpilrcema stgevacfge gihtaflkam lstgfkpqq giligiqqsf rprflgvaeg
1381 lhnegfklfa teatsdwl na nnpvtpvaw psqegqnpsl ssirkli rdg sidlvlnlpn
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```

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